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(FILE 'HOME' ENTERED AT 16:24:26 ON 02 FEB 2004)

FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, CAPLUS, BIOTECHDS' ENTERED AT
16:24:42 ON 02 FEB 2004

L1 4462 S MESENCHYMAL AND STROMAL AND CELL#
L2 585627 S CONTAINER OR CHAMBER OR HOUSE OR HOUSING OR BIOCOMPATIBLE
L3 31 S L2 AND L1
L4 17 DUP REM L3 (14 DUPLICATES REMOVED)
L5 359 S L1 AND SAME
L6 128 DUP REM L5 (231 DUPLICATES REMOVED)
L7 283 S L1 AND DEFINED
L8 96 DUP REM L7 (187 DUPLICATES REMOVED)

L8 ANSWER 74 OF 96 MEDLINE on STN DUPLICATE 55
AN 93092087 MEDLINE
DN 93092087 PubMed ID: 1458438
TI Ultrastructural analysis of differentiation of rat endoderm in vitro.
Adipose vascular-stromal cells induce endoderm differentiation, which in turn induces differentiation of the vascular-stromal cells into chondrocytes.
AU Loncar D
CS Department of Molecular Pathology, Medical School, University of California, Davis.
SO JOURNAL OF SUBMICROSCOPIC CYTOLOGY AND PATHOLOGY, (1992 Oct) 24 (4) 509-19.
Journal code: 8804312. ISSN: 1122-9497.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
ED Entered STN: 19930129
Last Updated on STN: 20000303
Entered Medline: 19930114
AB Isolated definitive endoderm from 9-day-old rat embryos was cultivated up to 24 days in plastic and glass petri dishes and on developing vascular-stromal cells (mesenchymal cells) from epididymal white and interscapular brown adipose tissue of 4-week-old male rats. Explants were analyzed histologically and ultrastructurally. Endoderm attached to the bottom of the glass or petri dishes degenerated under one week of cultivation. Endoderm free floating in the culture medium developed into unilaminar vesicles whose flat epithelium did not differentiate. However, endoderm inoculated on developing mesenchymal cells differentiated into glandular explants or into ciliated pseudostratified columnar respiratory epithelium. The glandular explants were made up of at least four different kinds of cells whose cytoplasm showed predominantly: a) polyribosomes, b) lysosomes, c) mitochondria or d) cytoskeletal filaments. Endodermal cells differentiated only if, during cultivation, they were in contact with or in close proximity to developing mesenchymal cells. Endoderm differentiating into the respiratory epithelium in turn directed differentiation of the underlying vascular-stromal cells into lamina propria cells and chondrocytes. Cultivated vascular-stromal cells in the upper layers became thicker, ellipsoid in shape and with enlarged intercellular space. They appeared to be lamina propria cells and, together with the respiratory epithelium, built folds of respiratory mucosa. The vascular-stromal cells in the layers close to the bottom developed into chondrocytes; i.e., the cells became oval and agglomerated in nest like structures with a defined extracellular matrix. Their cytoplasm contained abundant cisternae of rough endoplasmic reticulum and numerous vacuoles with PAS positive substance. These observations showed that even developing vascular-stromal cells from adipose tissue from postlactating rats can trigger the process of definitive endoderm differentiation. Once triggered, differentiating endoderm influenced differentiation of the vascular-stromal cells into the cells and tissues of a wall of the respiratory tract.

L8 ANSWER 65 OF 96 MEDLINE on STN DUPLICATE 48
AN 95354760 MEDLINE
DN 95354760 PubMed ID: 7628536
TI A chemically **defined** medium supports *in vitro* proliferation and maintains the osteochondral potential of rat marrow-derived **mesenchymal** stem **cells**.
AU Lennon D P; Haynesworth S E; Young R G; Dennis J E; Caplan A I
CS Department of Biology, Case Western Reserve University, Cleveland, Ohio 44106-7080, USA.
SO EXPERIMENTAL CELL RESEARCH, (1995 Jul) 219 (1) 211-22.
Journal code: 0373226. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199509
ED Entered STN: 19950921
Last Updated on STN: 19970203
Entered Medline: 19950901
AB Among the **stromal** elements in mammalian and avian bone marrow there exists a pluripotent subset of **cells** which we refer to as **mesenchymal** stem **cells** (MSCs). These **cells** can be isolated and will proliferate in culture. When such subcultured **cells** are introduced into porous tricalcium phosphate-hydroxyapatite ceramic cubes and implanted subcutaneously into syngeneic or immunocompromised hosts, the passaged MSCs are observed to differentiate into bone and cartilage. Heretofore, those assays have been conducted with MSCs which had been maintained *in vitro* in serum-containing medium. A serum-free medium (RDM-F), which consists of insulin, 5 micrograms/ml, linoleic acid-bovine serum albumin, 0.1%, platelet-derived growth factor-BB, 10 ng/ml, and basic fibroblast growth factor, 1 ng/ml in a base medium of 60% Dulbecco's modified Eagle's medium with low glucose and 40% MCDB-201, has been developed for rat marrow-derived MSCs. Proliferation rates of MSCs maintained in RDM-F equal those of **cells** maintained in serum-containing medium through Day 4 following subculturing and continue at up to 80% of the rate of the latter through Day 8 of subculture. When tested in the *in vivo* ceramic cube assay, MSCs cultured in RDM-F retain their osteochondral potential and differentiate into bone and cartilage in a manner indistinguishable from those cultivated in serum-containing medium. Utilization of this serum-free medium will facilitate analysis of the effects of other growth factors and cytokines on the proliferation and differentiation of MSCs, without the complexity of exogenous serum.

L8 ANSWER 1 OF 96 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:988016 CAPLUS
TI Bone marrow **mesenchymal** stem **cells**
AU Dennis, James E.; Caplan, Arnold I.
CS Department of Biology, Skeletal Research Center, Case Western Reserve
University, Cleveland, OH, USA
SO Stem Cells Handbook (2004), 107-117. Editor(s): Sell, Stewart. Publisher:
Humana Press Inc., Totowa, N. J.
CODEN: 69EWLW; ISBN: 1-58829-113-8
DT Conference
LA English
AB The term **mesenchymal** stem **cell** (MSC) refers to adult
mesenchymal progenitor **cells** with the potential to
produce progeny that differentiate to produce a variety of
mesenchymal **cell** types (e.g., fibroblasts, muscle, bone,
tendon, ligament adipose tissue). It is not known if these **cells**
actually have the capacity to self-renew, which is a property of stem
cells. MSCs may be found in muscle, skin, and adipose tissue, as
well as in the bone marrow. MSCs in the bone marrow may be identified by
colony-forming units that produce fibroblasts and make up a very small
percentage of the total marrow population. The ability of MSCs in the
bone marrow to form bone and cartilage has been known for more than 100
yr. MSCs or their progeny in the bone marrow provide a **stromal**
microenvironment for hematopoiesis. During development, MSCs in the bone
marrow may derive from the developing vessels (pericytes) or from
circulating precursors. MSCs also produce osteoclasts and osteoblasts
responsible for remodeling of bone and adipocytes, which make up a major
portion of the bone marrow. MSCs may be isolated from bone marrow,
peripheral blood, fat, skin, vasculature, and muscle, where they most
likely are responsible for normal tissue renewal, as well as for a
response to injury. Bone marrow MSCs are neg. for primitive hematopoietic
cell markers but express antibody-**defined** markers: SH2
(type III TGF receptor), SH3 and SH4 (ecto-5'-nucleotidase), and STRO-1.
Individual clones of **cell** lines derived from MSCs have different
potentials for differentiation, indicating different stages of detn. and
levels of plasticity. Transplanted MSCs have been shown to enhance bone,
tendon, cartilage, and nerve repair in exptl. models. Systemic
transplantation of MSCs has not always led to functional results in tissue
repair but has tremendous potential. The use of MSCs for gene therapy for
hematopoietic, metabolic, and neurol. disorders is currently under
investigation.

L8 ANSWER 18 OF 96 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:293990 BIOSIS
DN PREV200200293990
TI Methods of making conditioned **cell** culture medium compositions.
AU Naughton, Gail K. [Inventor, Reprint author]; Mansbridge, Jonathan N.
[Inventor]; Pinney, R. Emmett [Inventor]
CS La Jolla, CA, USA
ASSIGNEE: Advanced Tissue Sciences, Inc.
PI US 6372494 April 16, 2002
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Apr. 16, 2002) Vol. 1257, No. 3. <http://www.uspto.gov/web/menu/patdata.html>. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DT Patent
LA English
ED Entered STN: 15 May 2002
Last Updated on STN: 15 May 2002
AB Novel products comprising conditioned **cell** culture medium compositions and methods of use are described. The conditioned **cell** medium compositions of the invention may be comprised of any known **defined** or **undefined** medium and may be conditioned using any eukaryotic **cell** type. The medium may be conditioned by **stromal cells**, **parenchymal cells**, **mesenchymal stem cells**, **liver reserve cells**, **neural stem cells**, **pancreatic stem cells** and/or **embryonic stem cells**. Additionally, the **cells** may be genetically modified. A three-dimensional tissue construct is preferred. Once the **cell** medium of the invention is conditioned, it may be used in any state. Physical embodiments of the conditioned medium include, but are not limited to, liquid or solid, frozen, lyophilized or dried into a powder. Additionally, the medium is formulated with a pharmaceutically acceptable carrier as a vehicle for internal administration, applied directly to a food item or product, formulated with a salve or ointment for topical applications, or, for example, made into or added to surgical glue to accelerate healing of sutures following invasive procedures. Also, the medium may be further processed to concentrate or reduce one or more factors or components contained within the medium.

L6 ANSWER 4 OF 128 MEDLINE on STN DUPLICATE 2
AN 2003281001 IN-PROCESS
DN PubMed ID: 12783985
TI Formation of a chondro-osseous rudiment in micromass cultures of human bone-marrow **stromal cells**.
AU Muraglia Anita; Corsi Alessandro; Riminucci Mara; Mastrogiovanni Maddalena; Cancedda Ranieri; Bianco Paolo; Quarto Rodolfo
CS Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy.
SO Journal of cell science, (2003 Jul 15) 116 (Pt 14) 2949-55.
Journal code: 0052457. ISSN: 0021-9533.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030617
Last Updated on STN: 20031218
AB Bone-marrow **stromal cells** can differentiate into multiple **mesenchymal** lineages including cartilage and bone. When these **cells** are seeded in high-density 'pellet culture', they undergo chondrogenesis and form a tissue that is morphologically and biochemically defined as cartilage. Here, we show that dual chondro-osteogenic differentiation can be obtained in the **same** micromass culture of human bone-marrow **stromal cells**. Human bone-marrow **stromal cells** were pellet cultured for 4 weeks in chondro-inductive medium. Cartilage 'beads' resulting from the micromass culture were then subcultured for further 1-3 weeks in osteo-inductive medium. This resulted in the formation of a distinct mineralized bony collar around hyaline cartilage. During the chondrogenesis phase, type I collagen and bone sialoprotein were produced in the outer portion of the cartilage bead, which, upon subsequent exposure to beta-glycerophosphate, mineralized and accumulated extracellular bone sialoprotein and osteocalcin. Our modification of the pellet culture system results in the formation of a chondro-osseous 'organoid' structurally reminiscent of pre-invasion endochondral rudiments, in which a bony collar forms around hyaline cartilage. The transition from a **cell** culture to an organ culture dimension featured by our system provides a suitable model for the dissection of molecular determinants of endochondral bone formation, which unfolds in a precisely defined spatial and temporal frame

L4 ANSWER 3 OF 17 MEDLINE on STN
AN 2003189360 MEDLINE
DN 22594258 PubMed ID: 12708654
TI Bone marrow **stromal cells** and their use in
regenerating bone.
AU Cancedda Ranieri; Mastrogiacomo Maddalena; Bianchi Giordano; Derubeis
Anna; Muraglia Anita; Quarto Rodolfo
CS Istituto Nazionale per la Ricerca sul Cancro, Centro Biotecnologie
Avanzate, Universita di Genova, Largo R. Benzi 10, 16132 Genova, Italy.
SO NOVARTIS FOUNDATION SYMPOSIUM, (2003) 249 133-43; discussion 143-7, 170-4,
239-41. Ref: 29
Journal code: 9807767.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200306
ED Entered STN: 20030424
Last Updated on STN: 20030619
Entered Medline: 20030618
AB Tissue engineering approaches have recently been devised to repair large
bone losses. Tissue engineering takes advantages of the combined use of
cultured living **cells** and 3D scaffolds to deliver vital
cells to the damaged site of the patient. Cultured bone marrow
stromal cells (BMSCs) can be regarded as a
mesenchymal progenitor/precursor **cell** population derived
from adult stem **cells**. When implanted in immunodeficient mice,
BMSCs combined with mineralized 3D scaffolds to form a primary bone tissue
that is highly vascularized. We have used autologous BMSC/bioceramic
composites to treat full-thickness gaps of tibial diaphysis in sheep. The
healing process has been investigated. The sequence of events is as
follows: (1) bone formation on the outer surface of the implant; (2) bone
formation in the inner cylinder canal; (3) formation of fissures and
cracks in the implant body; (4) bone formation in the bioceramic pores.
Similar composites whose size and shape reflected each bone defect have
been implanted at the lesion sites of three patients. External fixation
was used. Patients have been followed for more than three years. The
results obtained are very promising and we propose the use of
culture-expanded osteoprogenitor **cells** in conjunction with
hydroxyapatite bioceramics as a significant improvement in the repair of
critical size long bone defects.

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